

We claim:

1. An isolated nucleic acid molecule encoding a PAAD-containing polypeptide, comprising:
 - 5 (a) a nucleic acid molecule encoding a polypeptide comprising the amino acid sequence set forth as SEQ ID NOs: 16, 18, 20, 22, 24, 26 or 28; or
 - 10 (b) a nucleic acid molecule that hybridizes to the nucleic acid molecule of (a) under highly stringent conditions, where the nucleic acid molecule encodes a biologically active PAAD domain-containing polypeptide.
- 15 2. The nucleic acid molecule of claim 1, comprising a nucleotide sequence set forth as any of SEQ ID NO: 15, 17, 19, 21, 23, 25 and 27.
- 20 3. A vector containing the nucleic acid molecule of claim 1.
4. A recombinant cell containing the nucleic acid molecule of claim 1.
- 25 5. An isolated nucleic acid molecule encoding a PAAD domain, comprising:
 - (a) a nucleic acid molecule encoding a PAAD domain amino acid sequence set forth as any of SEQ ID NOS: 2, 3, 4, 5, 6, 8, or 10; or
 - 30 (b) a nucleic acid molecule that hybridizes to the nucleic acid molecule of (a) under highly stringent conditions, where the nucleic acid

molecule encodes a biologically active PAAD domain.

7. A vector containing the nucleic acid molecule
5 of claim 6.

8. A recombinant cell containing the nucleic acid molecule of claim 6.

10 9. An isolated nucleic acid molecule encoding an NB-ARC domain, comprising:

(a) a nucleic acid molecule encoding the NB-ARC domain amino acid set forth as any of SEQ ID NOS:37, 60, 62 or 63;

15 (b) a nucleic acid molecule that hybridizes to the nucleic acid molecule of (a) under highly stringent conditions, where the nucleic acid molecule encodes a biologically active NB-ARC domain.

20 10. A vector containing the nucleic acid molecule of claim 9.

11. A recombinant cell containing the nucleic acid molecule of claim 9.

12. An isolated nucleic acid molecule encoding an LRR domain, comprising:

30 (a) a nucleic acid molecule encoding the LRR domain amino acid set forth as any of SEQ ID NOS:39, 61 or 64; or

(b) a nucleic acid molecule that hybridizes to the nucleic acid molecule of (a) under highly

stringent conditions, where the nucleic acid molecule encodes a biologically active LRR domain.

13. A vector containing the nucleic acid molecule
5 of claim 12.

14. A recombinant cell containing the nucleic acid molecule of claim 12.

10 15. An oligonucleotide comprising at least 17 nucleotides capable of specifically hybridizing with the nucleotide sequence set forth in any of SEQ ID NOS:15, 17, 19, 21, 23, 25 and 27 or the complement thereof.

15 16. An oligonucleotide comprising at least 50 nucleotides capable of specifically hybridizing with the nucleotide sequence set forth in any of SEQ ID NOS:15, 17, 19, 21, 23, 25 and 27 or the complement thereof.

20 17. An isolated PAAD domain-containing polypeptide, comprising an amino acid sequence at least 80% identical to the amino acid sequence set forth in any of SEQ ID NOS:16, 18, 20, 22, 24, 26 or 28, wherein said polypeptide is a biologically active PAAD domain-containing
25 polypeptide.

18. The PAAD domain-containing polypeptide of claim 17, wherein said polypeptide comprises the amino acid sequence set forth as any of SEQ ID NOS:16, 18, 20, 22, 24,
30 26 or 28.

19. An isolated PAAD domain polypeptide,
comprising an amino acid sequence at least 80% identical to
the amino acid sequence set forth as any of SEQ ID NOS: 2,
3, 4, 5, 6, 8, or 10, wherein said polypeptide is a
5 biologically active PAAD domain polypeptide.

20. An isolated PAAD domain polypeptide,
comprising the amino acid sequence set forth as any of SEQ
ID NOS: 2, 3, 4, 5, 6, 8, or 10.

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21. An isolated NB-ARC domain polypeptide,
comprising an amino acid sequence at least 80% identical to
the amino acid sequence set forth as any of SEQ ID NOS:37,
60, 62 or 63, wherein said polypeptide is a biologically
15 active NB-ARC domain polypeptide.

22. An isolated NB-ARC domain polypeptide,
comprising an amino acid sequence set forth as any of SEQ
ID NOS:37, 60, 62 or 63.

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23. An isolated LRR domain polypeptide,
comprising an amino acid sequence at least 80% identical to
the amino acid sequence set forth as any of SEQ ID NOS:39,
61 or 64, wherein said polypeptide is a biologically active
25 LRR domain polypeptide.

24. An isolated LRR domain polypeptide,
comprising an amino acid sequence set forth as any of SEQ ID
NOS:39, 61 or 64.

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25. An isolated peptide comprising at least 10
contiguous amino acids of any of SEQ ID NOS:16, 18, 20, 22,
24, 26 or 28.

26. A method of producing a PAAD domain-containing polypeptide comprising expressing the nucleic acid molecule of claim 1 *in vitro* or in a cell under conditions suitable for expression of said polypeptide.

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27. An isolated anti-PAAD antibody having specific reactivity with the PAAD domain-containing polypeptide of claim 18.

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28. The antibody of claim 27, wherein said antibody is a monoclonal antibody.

29. A cell line producing the monoclonal antibody of claim 29.

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30. The antibody of claim 27, wherein said antibody is a polyclonal antibody.

31. A method of identifying a nucleic acid molecule encoding a PAAD-containing polypeptide in a sample, said method comprising:

contacting a sample containing nucleic acids with an oligonucleotide according to claim 15, wherein said contacting is effected under high stringency hybridization conditions, and identifying a nucleic acid molecule which hybridizes thereto.

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32. A method of detecting the presence of a PAAD domain-containing polypeptide in a sample, said method comprising contacting a test sample with an antibody
5 according to claim 27, detecting the presence of an antibody:polypeptide complex, and thereby detecting the presence of a PAAD domain-containing polypeptide in said test sample.

10 33. A method of identifying a PAAD domain-containing polypeptide-associated polypeptide (PAP) comprising the steps of:

- (a) contacting the PAAD domain-containing polypeptide of claim 17 with a candidate PAP;
- 15 (b) detecting association of said PAAD domain-containing polypeptide with said candidate PAP,
wherein a candidate PAP that associates with said polypeptide is identified as a PAP.

20 34. A method of identifying a PAP comprising the steps of:

- (a) contacting the PAAD domain polypeptide of claim 19 with a candidate PAP;
- (b) detecting association of said PAAD domain
25 polypeptide with said candidate PAP,
wherein a candidate PAP that associates with said polypeptide is identified as a PAP.

30 35. A method of identifying a PAP comprising the steps of:

- (a) contacting the NB-ARC domain polypeptide of claim 21 with a candidate PAP;

(b) detecting association of said NB-ARC polypeptide with said candidate PAP,

wherein a candidate PAP that associates with said polypeptide is identified as a PAP.

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36. A method of identifying a PAP comprising the steps of:

(a) contacting the LRR domain polypeptide of claim 23 with a candidate PAP;

10 (b) detecting association of said LRR polypeptide with said candidate PAP,

wherein a candidate PAP that associates with said polypeptide is identified as a PAP.

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37. A method of identifying an effective agent that alters the association of a PAAD domain-containing polypeptide with a PAAD domain-containing polypeptide-associated polypeptide (PAP), comprising the steps of:

20 (a) contacting the PAAD domain-containing polypeptide of claim 17, or a PAAD, NB-ARC or LRR domain therefrom, and said PAP under conditions that allow said PAAD domain-containing polypeptide or said fragment and said PAP to associate, with a candidate agent; and

25 (b) detecting the altered association of said PAAD domain-containing polypeptide or domain with said PAP,

wherein an agent that alters said association is identified as an effective agent.

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38. The method of claim 37, wherein said PAP is selected from the group consisting of ASC, ASC2, Caspase-1, Card10, Nod1, NIK, IKK-i, IkB α and IKAP.

39. A method of identifying an agent that associates with a PAAD domain-containing polypeptide, comprising the steps of:

- 5 (a) contacting the PAAD domain-containing polypeptide of claim 17 with a candidate agent; and
 (b) detecting association of said PAAD domain-containing polypeptide with said agent.

10 40. A method of identifying an agent that associates with a PAAD domain polypeptide, comprising the steps of:

- (a) contacting the PAAD domain polypeptide of claim 19 with a candidate agent; and
15 (b) detecting association of said PAAD domain polypeptide with said agent.

 41. A method of identifying an agent that associates with a NB-ARC domain polypeptide, comprising the
20 steps of:

- (a) contacting the NB-ARC domain polypeptide of claim 21 with a candidate agent; and
 (b) detecting association of said NB-ARC domain polypeptide with said agent.

25 42. A method of identifying an agent that associates with a LRR domain polypeptide, comprising the steps of:

- (a) contacting the LRR domain polypeptide of claim 23 with a candidate agent; and
30 (b) detecting association of said LRR domain polypeptide with said agent.

43. A method of identifying an agent that modulates PAAD domain-mediated inhibition of NFkB activity, comprising the steps of:

- (a) contacting a cell that recombinantly
5 expresses a PAAD domain-containing polypeptide with a candidate agent; and
- (b) detecting NFkB activity in said cell,
whereas increased or decreased NFkB activity in said cell
compared to a control cell indicates that said candidate
10 agent is an agent that modulates PAAD domain-mediated inhibition of NFkB activity.

44. The method of claim 43, wherein said PAAD domain polypeptide comprises an amino acid sequence set
15 forth as any of SEQ ID NOS:1-14.

45. The method of claim 43, wherein said PAAD domain polypeptide comprises an amino acid sequence at least 80% identical to the amino acid sequence set forth as any of
20 SEQ ID NOS: 2, 3, 4, 5, 6, 8, or 10, wherein said polypeptide is a biologically active PAAD domain polypeptide.

46. The method of claim 43, wherein said cell is
25 contacted with or recombinantly expresses an inducer of NFkB activity.

47. A method of identifying an agent that modulates an activity of a NB-ARC domain of a PAAD domain-
30 containing polypeptide, comprising the steps of:

- (a) contacting the NB-ARC domain polypeptide of claim 21 with a candidate agent; and

(b) detecting an activity of said NB-ARC domain, whereby an increase or decrease of said activity identifies said agent as an agent that modulates the activity of the NB-ARC domain of said PAAD

5 domain-containing polypeptide;

wherein the detected activity of said NB-ARC domain is selected from homo-oligomerization, hetero-oligomerization, nucleotide hydrolysis, and nucleotide binding.

10 48. A method of modulating NFkB transcriptional activity in a cell, comprising the steps of:

(a) introducing the nucleic acid molecule of claim 5 into a cell; and

15 (b) expressing said nucleic acid molecule in said cell, whereby the expression of said nucleic acid modulates NFkB transcriptional activity in said cell.

20 49. A method of decreasing expression of a PAAD domain-containing polypeptide in a cell, comprising introducing an antisense or dsRNA nucleic molecule into a cell, wherein said antisense or dsRNA nucleic molecule binds to any of SEQ ID NOS:15, 17, 19, 21, 23, 25 and 27.

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